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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/336,266	06/14/1999	GUY W. BEMIS	VPI/96-16.CI	7430

7590 03/05/2002

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EXAMINER

RAO, DEEPAK R

ART UNIT	PAPER NUMBER
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1624

DATE MAILED: 03/05/2002

15

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.
09/336,266

Applicant(s)
Bemis et al.

Examiner
Deepak Rao

Art Unit
1624



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Feb 8, 2002
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 4-12, 15, 24-38, 46-48, and 62-67 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 46-48, 62, 64, and 66 is/are allowed.
- 6) ☒ Claim(s) 4-12, 15, 24-38, 63, 65, and 67 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- *See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892) 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 19) ☐ Notice of Informal Patent Application (PTO-152)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 20) ☐ Other:

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DETAILED ACTION

This office action is in response to the amendment filed on February 8, 2002. The amendment has been entered. Claims 38, 4-12, 15, 24-37, 46-48 and 62-67 are currently pending in this application.

Upon reconsideration, the finality of that action is withdrawn and the following rejections are made under new grounds:

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 26-37, 63, 65 and 67 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of most of the diseases listed in claim 26, does not reasonably provide enablement for treating inflammatory diseases, infectious diseases, proliferative diseases, neurodegenerative diseases, viral diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to the invention commensurate in scope with these claims.

The specification, while enabling for treating some of the diseases, fails to enable one skilled in the art to use the instantly claimed compounds in treating the laundry list of disorders recited in the instant claims. The use disclosed in the specification is as p38 inhibitors useful to

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treat a variety of diseases, see specification pages 1-2. Biological assays to test the activity of the compounds are provided on pages 94-109 and the p38 inhibitory activity of the compounds is further confirmed by the Declaration by Dr. Bemis. However, there is no correlation provided how this inhibitory effect is useful in treating a myriad of diseases recited in the instant claims.

The claims are drawn to a method of treating a myriad of diseases with different etiologies such as inflammatory diseases, autoimmune diseases, viral diseases, proliferative diseases, neurodegenerative diseases, etc. It is inconceivable as to how the claimed single class of compounds can treat the laundry list of diseases recited in the claims having diverse mechanisms. Enablement for the scope of treating 'inflammatory diseases' generally is not present. For a compound or a genus to be effective against all inflammatory diseases is contrary to medical science. Inflammation is a process which can take place in virtually any site or any part of the body. There is no common mechanism by which all, or even most inflammatory diseases arise. Mediators include bradykinin, serotonin, histamine, leukotriene, cytokine, and many others. Accordingly, treatments for inflammatory diseases are normally tailored to the particular type of inflammation, and there is no "magic bullet" against inflammatory disease generally.

"Neurodegenerative diseases" cover broad array of diseases having diverse modes of action, origin, mechanism, etc. For example, 'neurodegenerative diseases' covers diverse disorders some of which are listed in the specification, page 54, lines 22-26. The term, however, covers many other diseases such as hereditary cerebellar ataxias, paraplegias, syringomyelia,

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phakomatoses, and much more. In fact, Layzer, Cecil Textbook of Medicine (article enclosed), states that “some degenerative diseases are difficult to classify because they involve multiple anatomic locations” (see page 2050). Neurodegenerative disease such as Alzheimer’s disease has no known cause and has been treated mostly by choline esterase inhibitors to prolong the activity of acetylcholine.

A viral disease such as HIV infection has been known to be treated with a nucleoside analog or a protease inhibitor to disrupt the production of viral protein or DNA.

There is no such agent which can treat ‘infectious diseases’ generally. The recitation is extremely broad. Some infectious diseases are caused by bacteria (e.g., meningitis, whooping cough, tetanus, syphilis, etc.), some are caused by virus (e.g., HIV, common cold, measles, chicken pox, etc.), some due to fungus (e.g., athlete’s foot, etc.), some are caused by protozoa (e.g., amebiasis, giardiasis, leishmaniasis, etc.). Not only that the viral diseases different from bacterial or fungal diseases, but the viral diseases are also different one from the other. The nature of effect, origin, symptom, incubation, diagnosis, etc. is different for each one from the other. The same is true for other ‘infectious diseases’ embraced by the instant claims.

A ‘proliferative disorder’ is anything that causes abnormal tissue growth. That can be growth by cellular proliferation more rapidly than normal, or continued growth after the stimulus that initiated the new growth has ceased, or lack (partial or complete) of structural organization and/or coordination with surrounding tissue. It can be benign or malignant. Thus, such term covers not only all cancers, but also covers precancerous conditions such as lumps, lesions,

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polyps, etc. No compound has ever been found to cancers of all types generally. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. The existence of such a "silver bullet" is contrary to our present understanding of oncology. Cecil Textbook of Medicine states that "each specific type has unique biologic and clinical features that must be appreciated for proper diagnosis, treatment and study" (see the enclosed article, page 1004). Different types of cancers affect different organs and have different methods of growth and harm to the body. Also see *In re Buting*, 163 USPQ 689 (CCPA 1969), wherein 'evidence involving a single compound and two types of cancer, was held insufficient to establish the utility of the claims directed to disparate types of cancers'. Thus, it is beyond the skill of oncologists today to get an agent to be effective against cancers generally.

(Only a few of the claimed diseases are discussed here to make the point of an insufficient disclosure, it does not definitely mean that the other diseases meet the enablement requirements). The state of the art reference provided in the specification WO 95/31451 (page 2, line 25) is drawn to a different class of compounds and also does not relate to p38 inhibitory activity. The references cited in PTO-1449, teach that **antiarthritic** activity was observed for p38 kinase inhibitor, see Badger et al. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general and the lack of working examples commensurate in scope with the claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the methods of treating instantly claimed.

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The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 38, 4-12, 15 and 24-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

1. In claim 38, in the definition of heterocyclic ring (see last 3 lines), the term "comprises" is open ended. 'Comprises' in a compound claim, leaves the claim open for the inclusion of unspecified groups and/or substituents. The use of the above phrase causes the claim to be broader than the invention. See *In re Fenton*, 451 F.2d 640, 171 USPQ 693 (CCPA 1971). Replacing the term with -- consists of -- (in all occurrences) is suggested.
2. In claim 24, the structural formula of compound # 406 is incomplete, see at the 4-position of the phenyl ring the term "CH" should be -- CH₃ -- as per the structure provided in the specification at page 51.

The other claims are included here because they are dependent claims and do not resolve the above issues.

Allowable Subject Matter

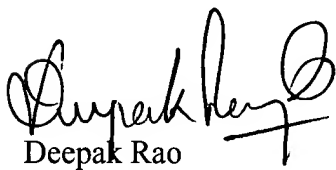
Claims 38, 4-12, 15, 24 and 25 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action.

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Claims 46-48, 62, 64 and 66 are allowed. The references of record do not teach or fairly suggest the instantly claimed compounds.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (703) 305-1879. The examiner can normally be reached on Tuesday-Friday from 6:30am to 5:00pm. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

A handwritten signature in black ink, appearing to read 'Deepak Rao', with a stylized flourish at the end.

Deepak Rao
February 28, 2002